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| 10/581,144 | 07/05/2007 | Christian Belmant | INN-135 | 1963 |

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| EXAMINER | |
|---|---|
| LAU, JONATHAN S | |

| ART UNIT | PAPER NUMBER |
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| 1623 | |

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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

euspto@slspatents.com

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/581,144 | BELMANT ET AL. | |
| | Examiner | Art Unit | |
| | Jonathan S. Lau | 1623 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *22 September 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *23-26 and 31-37* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *23-26 and 31-37* is/are allowed.

6)☒ Claim(s) *31-35* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *1 pg / 22 Sep 2009*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

This Office Action is responsive to Applicant's Amendment and Remarks, filed 22 Sep 2009, in which claims 23 and 25 are amended to change the scope and breadth of the claim, claims 27-30 are canceled, claims 24 and 26 are amended to change dependency, new claims 36 and 37 are added, and withdrawn claim 31 is amended.

This application is the national stage entry of PCT/IB04/04311, filed 02 Dec 2004; and claims benefit of provisional application 60/579,237, filed 15 Jun 2004; and claims benefit of foreign priority document PCT/IB03/06375, filed 02 Dec 2003. This foreign priority document is in English.

Claims 23-26 and 31-37 are pending in the current application. Claims 31-35, drawn to non-elected inventions, are rejoined. Claims 23-26 and 31-37 are examined on the merits herein.

### *Election/Restrictions*

Claims 23-26 and new claims 36 and 37 are allowable. The restriction requirement between groups V and XII, as set forth in the Office action mailed on 22 Sep 2008, has been reconsidered in view of the allowability of claims to the elected invention pursuant to MPEP § 821.04(a). **The restriction requirement is hereby withdrawn as to any claim that requires all the limitations of an allowable claim.** Claims 27-35, directed to a method of activating T cells or stimulating an immune

response comprising administering a compound according to general Formula (I) is no longer withdrawn from consideration because the claim(s) requires all the limitations of an allowable claim.

In view of the above noted withdrawal of the restriction requirement, applicant is advised that if any claim presented in a continuation or divisional application is anticipated by, or includes all the limitations of, a claim that is allowable in the present application, such claim may be subject to provisional statutory and/or nonstatutory double patenting rejections over the claims of the instant application.

Once a restriction requirement is withdrawn, the provisions of 35 U.S.C. 121 are no longer applicable. See *In re Ziegler*, 443 F.2d 1211, 1215, 170 USPQ 129, 131-32 (CCPA 1971). See also MPEP § 804.01.

***Objections Withdrawn***

Applicant's Amendment, filed 22 Sep 2009, with respect to objection to the claims has been fully considered and is persuasive, as claim 23 is amended to correct the informality.

This rejection has been **withdrawn**.

***Rejections Withdrawn***

Applicant's Amendment, filed 22 Sep 2009, with respect to claims 23-26 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement has been fully considered and is persuasive, as amended

claims 23 and 25 recites the invention as reasonably conveyed to one skilled in the relevant art that the inventors, at the time the application was filed, had possession.

This rejection has been **withdrawn**.

Applicant's Remarks, filed 22 Sep 2009, with respect to claims 23 and 26 rejected under 35 U.S.C. 103(a) as being unpatentable over Fox et al. (J. Org. Chem., 2002, 67, p5009-5010, of record) in view of Patini et al. (Chem. Rev. 1996, 96, p3147-3176, of record) and in view of Parvin et al. (Biochemistry, 1969, 8(4), p1748-1755, of record) has been fully considered and is persuasive, as Applicant's showing of unexpectedly advantageous results commensurate with the scope of the claim compared to the teaching of the prior art teaching bioisoteric equivalence is persuasive in view of the unpredictability in the art.

This rejection has been **withdrawn**.

Applicant's Remarks, filed 22 Sep 2009, with respect to claims 24 and 25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Fox et al. (J. Org. Chem., 2002, 67, p5009-5010, of record) in view of Patini et al. (Chem. Rev. 1996, 96, p3147-3176, of record) and in view of Parvin et al. (Biochemistry, 1969, 8(4), p1748-1755, of record) as applied to claims 23 and 26 above, and further in view of Sicard et al. (Infection and Immunity, 2000, 68(8), p4375-4377, of record) and Cox et al. (Vaccine, 1997, 15(3), p248-256, of record) has been fully considered and is persuasive, as Applicant's showing of unexpectedly advantageous results commensurate with the

scope of the claim compared to the teaching of the prior art teaching bioisoteric equivalence is persuasive in view of the unpredictability in the art.

This rejection has been **withdrawn**.

The following are new grounds of rejection necessitated by Applicant's Amendment, filed 22 Sep 2009, in which claims 23 and 25 are amended to change the scope and breadth of the claim, claims 27-30 are canceled, claims 24 and 26 are amended to change dependency, new claims 36 and 37 are added, and withdrawn claim 31 is amended; and resulting in rejoinder of claims 31-35, drawn to non-elected inventions.

***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Amended Claims 31-35 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. Claims 31 and 33 recite "Cat+ represents ... organic or mineral cation(s) including proton". Claims 32 and 34 depend from claim 31 and 33 and incorporate all limitations therein. Claim 35 recites "antigen".

The specification discloses chemicals, such as the cations $H^+$, $Na^+$, $NH_4^+$, $K^+$, $Li^+$,

trimethylamine, lysine, and any other pharmaceutically acceptable cations at page 15, lines 15-16 which meet the written description and enablement provisions of 35 USC 112, first paragraph. However, claims 23-26 are directed to encompass organic or mineral cation(s), which only correspond in some undefined way to specifically instantly disclosed chemicals. None of these cations meet the written description provision of 35 USC § 112, first paragraph, due to lacking chemical structural information for what they are and because cations are highly variant and encompass a myriad of possibilities. The specification provides insufficient written description to support the genus encompassed by the claim. The specification provides only non-limiting examples of the preferred embodiments, such as the well-defined group of pharmaceutically acceptable cations at page 15, lines 15-16.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention.* The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.)

The recitation “antigen” is seen to be merely functional language. The terms “antigen” defines a compound solely by its function in an organism, and does not necessarily convey structural information.

Functional language at the point of novelty, as herein employed by Applicants, is admonished in *University of California v. Eli Lilly and Co.* 43 USPQ2d 1398 (CAFC,

1997) at 1406: stating this usage does "little more than outline goal appellants hope the recited invention achieves and the problems the invention will hopefully ameliorate". The CAFC further clearly states that "[A] written description of an invention involving a chemical genus, like a description of a chemical species, requires a precise definition, such as by structure, formula, [or] chemical name, of the claimed subject matter sufficient to distinguish it from other materials" at 1405(emphasis added), and that "It does not define any structural features commonly possessed by members of the genus that distinguish from others. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus. A definition by function, as we have previously indicated, does not suffice to define the genus.." at 1406 (emphases added).

Thus, Applicants functional language at the points of novelty fails to meet the requirements set forth under 35 U.S.C. 112, first paragraph. Claims employing functional language at the exact point of novelty, such as Applicants', neither provide those elements required to practice the inventions, nor "inform the public during the life of the patent of the limited of monopoly asserted" (*General Electric Company v. Wabash Appliance Corporation et al.* 37 USPQ at 468 (US Supreme Court 1938)).

With the exception of the above specifically disclosed chemical structures, the skilled artisan cannot envision the detailed chemical structure of the encompassed cations or antigens, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. The chemical structure

itself is required. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016. In Fiddes v. Baird, 30 USPQ2d 1481, 1483, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. The specification provided only the bovine sequence. Finally, University of California v. Eli Lilly and Co., 43 USPQ2d 1398, 1404, 1405 held that:

> ...To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." *Lockwood v. American Airlines, Inc.*, 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); *In re Gosteli*, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) ("[T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." *Lockwood*, 107 F.3d at 1572, 41 USPQ2d at 1966.

Therefore, only the structurally defined chemical compounds, but not the full breadth of the claims, meet the written description provision of 35 USC § 112, first paragraph. The species specifically disclosed are not representative of the genus because the genus is highly variant. Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 USC § 112 is severable from its enablement provision. (See Vas-Cath at page 1115.)

The court of *In re Curtis* held that “a patentee will not be deemed to have invented species sufficient to constitute the genus by virtue of having disclosed a single species when… the evidence indicates ordinary artisans could not predict the operability … of any other species.” (see *In re Curtis* 354 F.3d 1347, 69 USPQ2d 1274,

Fed. Cir. 2004). The court of *Noelle v. Lederman* also pointed out that generic claim to anti-CD40CR Mabs lacked written description support because there was no description of anti-human or other species Mabs, and no description of human CD40CR antigen. The court further pointed out that attempt to "define an unknown by its binding affinity to another unknown" failed. See 355 F.3d 1343, 69 USPQ2d 1508, Fed. Cir. 2004.

Amended Claims 33-35 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for immunotherapy or stimulation of an immune response in a subject suffering from an infectious disease, does not reasonably provide enablement for immunotherapy or stimulation of an immune response in a subject in any subject or suffering from a tumor, solid tumor, or an autoimmune disease or an allergic disease. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The Applicant's attention is drawn to *In re Wands*, 8 USPQ2d 1400 (CAFC1988) at 1404 where the court set forth eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing *Ex parte Forman*, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors:

(1) The nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the claims; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

Nature of the invention: The nature of the invention are compounds of formulae (X), (XI) or (XII) for immunotherapy or stimulation of an immune response in a subject suffering from a tumor, solid tumor, an infectious disease or an autoimmune disease or an allergic disease.

The state of the prior art: The state of the prior art is Montero et al. (US Patent Application Publication 2006/0241087, provided by Applicant in IDS mailed 17 Aug 2007) disclosing phosphonate compounds of formula (I), see column 2, useful to modulate T lymphocyte activity. However, Montero et al. provides working examples of only T lymphocyte proliferation activity (examples 113-114 spanning pages 37-38).

Jomaa et al. (US Patent 7,399,756, provided by Applicant in IDS mailed 22 Sep 2009) teaches organo-phosphorous compounds for activating gamma/delta T cells (abstract). However, Jomaa et al. provides working examples of only T cell activation activity *in vitro* (column 15, lines 55-65 and column 16, lines 1-15).

The relative skill of those in the art: The relative skill of those in the art is high.

The predictability or unpredictability of the art: The sheer number of immunotherapies or stimulation of an immune response in any subject means that one skilled in the art cannot predict the usefulness for all possible immunotherapies or immune responses in any possible subject. Therefore the claimed invention is unpredictable.

The Breadth of the claims: The instant breadth of the rejected claims is broader than the disclosure, specifically, the instant claims include the method of administrating any compound of formulae (X), (XI) or (XII) for immunotherapy or stimulation of an

immune response in any possible subject, including but not limited to a subject suffering from a tumor, solid tumor, an infectious disease or an autoimmune disease or an allergic disease.

The amount of direction or guidance presented and the presence or absence of working examples:

The only direction or guidance present in the instant specification is the listing of Biological assay for testing cytokine (i.e., TNFα) release, see Example 5 on pages 43-44 of the specification. There are no *in vitro* or *in vivo* working examples present for the treatment of any cancer such as a tumor, solid tumor, or an autoimmune disease or an allergic disease by the administration of the instant invention.

The quantity of experimentation necessary:

The level of skill in the art is high. However, due to the unpredictability in the pharmaceutical art, it is to practice the claimed invention. Thus, factors such as "sufficient working examples", "the level of skill in the art" and "predictability", etc. have been demonstrated to be sufficiently lacking in the instantly claimed methods. In view of the breadth of the claim, the chemical nature of the invention, and the lack of working examples regarding the activity of the claimed compounds in regards to the treatment of the many tumors, one having ordinary skill in the art would have to undergo an undue amount of experimentation to use the invention commensurate in scope with the claims.

Genentech Inc. v. Novo Nordisk A/S (CA FC) 42 USPQ2d 1001, states that " a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion" and "patent protection is granted in return for an enabling

disclosure of an invention, not for vague intimations of general ideas that may or may not be workable".

Therefore, in view of the Wands factors and *In re Fisher* (CCPA 1970) discussed above, to practice the claimed invention herein, a person of skill in the art would have to engage in undue experimentation, with no assurance of success. It is noted that each embodiment of the invention is required to be individually assessed for physiological activity by *in vitro* and *in vivo* screening to determine which methods of use exhibit the desired pharmacological activity and which diseases would benefit from this activity. Thus, the specification fails to provide sufficient support of the broad use of the compounds of the instant claims for the treating cancer such as a tumor or solid tumor or an autoimmune disease or an allergic disease.

***Allowable Subject Matter***

Claims 23-26 and new claims 36 and 37 are allowable.

The closest prior art is Fox et al. (J. Org. Chem., 2002, 67, p5009-5010, of record) in view of Patini et al. (Chem. Rev. 1996, 96, p3147-3176, of record) and in view of Parvin et al. (Biochemistry, 1969, 8(4), p1748-1755, of record).

Fox et al. in view of Patini et al. and in view of Parvin et al. teach as set forth in the Office Action mailed 22 Jun 2009.

Applicant's showing of unexpectedly advantageous results commensurate with the scope of the claim compared to the teaching of the prior art teaching bioisoteric

equivalence is persuasive in view of the unpredictability in the art. Therefore the instant invention is not obvious over the teachings of Fox et al. in view of Patini et al. and in view of Parvin et al.

## *Conclusion*

Claims 23-26 and new claims 36 and 37 are allowable. Claims 31-35 are rejected.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jonathan S. Lau whose telephone number is 571-270-3531. The examiner can normally be reached on Monday - Thursday, 9 am - 4 pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shaojia Anna Jiang can be reached on 571-272-0627. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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